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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/574,386	05/19/2000	Donna G. Albertson	407E-914400US	7843

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EXAMINER	
SPIEGLER, ALEXANDER H	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 02/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/574,386	ALBERTSON ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-21 and 23-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-21 and 23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6/24/03
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

1. This action is in response to Paper No. 6, filed on October 15, 2003. Currently, claims 1, 3-21 and 23-25 are pending. All arguments have been fully considered and thoroughly reviewed, but are deemed not persuasive for the reasons that follow. This action is made FINAL. Any objections and rejections not reiterated below are hereby withdrawn.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1, 3-16, 20, 23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (US 5,807,522, cited in the IDS), in view of Smith (PCR Methods and Applications (1992) 2: 21-27, cited in the IDS).

Brown teaches methods for fabricating microarrays of biological samples. Specifically, Brown teaches a method for forming a microarray comprising, dispensing a known volume of a reagent at a selected array position, by tapping a capillary dispenser onto a support under conditions effective to draw a defined volume of liquid onto the support (abstract). Therefore, Brown teaches a method form forming grid arrays (i.e., microarrays) comprising placing

biological samples at discrete locations on said array (see cols. 3-5 and Figs 3-4 which teach the application of biological solutions to discrete locations on an array).

The reference teaches that the microarray can comprise immobilized polynucleotides (col. 11, 43-61 and col. 13 to col. 14, ln. 34). Brown teaches that these immobilized microarrays can be used for "large scale hybridizations assays in numerous genetic applications, including genetic and physical mapping of genomes, monitoring of gene expression, DNA sequencing, genetic diagnosis, genotyping of organisms", etc. (col. 14, ln. 35 to col. 15, ln. 67). Brown also teaches that his method overcomes limitations of prior methods to array genomic fragments (col. 1, ln. 64 to col. 2, ln. 25). In one embodiment, Brown teaches the application of target solutions comprising amplified products to one or more substrates, wherein each target solution is applied to a distinct location on one substrate to produce an array of polynucleotides (col. 16, ln. 23-38 and col. 17, ln. 45-55).

Furthermore, Brown reference teaches that the volume of each target applied to the substrate is 0.01 to 100 nanoliters (col. 3, ln. 39-41), and the array can comprises at least 10^3 amplification products in a 1 cm^2 region of substrate (col. 4, ln. 16-19).

Accordingly, Brown teaches a method of preparing an array of polynucleotides, including preparing an array of amplified polynucleotide products.

Brown does not teach preparing an array of specific PCR products, such as those from a ligation-mediated PCR reaction.

However, Smith teaches the advantages of carrying out a ligation-mediated PCR reaction. Specifically, Smith teaches the advantages of performing ligation-mediated PCR is that "specific fragments can be isolated without any prior knowledge of the nucleotide sequence of the target"

and furthermore, individual, unknown fragments can be amplified "from any DNA molecule ranging from about 50 to 250kb in size" (pg. 21).

Smith teaches ligation-mediated PCR of restriction fragments from large DNA molecules. Specifically, Smith teaches the method comprising,

a) providing a plurality of samples of double-stranded polynucleotide fragments, wherein each sample is derived from a first polynucleotide;

b) ligating adapters to each end of the polynucleotide fragments, wherein each adapter comprises a first strand and a second strand, the second strand having a region of substantial complementarity to a region of the first strand;

c) using sequences within the adapters to amplify the modified polynucleotide fragments to produce an amplification product for each sample of polynucleotide fragments, wherein each amplification product is representative of the first polynucleotide corresponding to each sample. (see abstract, pgs. 21-22, Table 1 and pg. 24)

Smith also teaches that the ligase-mediated PCR technique can be used in polynucleotides derived from large molecules, such as YAC (see abstract and pg. 25). With respect to claim 10, the reference teaches the use of a type IIS restriction endonuclease (see abstract). With respect to claims 11-13, the reference teaches that the length of the double stranded sequence is 350 basepairs. Finally, Smith teaches that his PCR products can be used in arraying high-density grids (e.g., polynucleotide arrays) (pg. 26).

In view of the teachings of Smith, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Brown so as to have included the steps of applying target solutions comprising amplification products from the

ligation-mediated PCR reaction of Smith, in order to have achieved the benefits stated by Smith of providing an effective means of analyzing unknown DNA from large molecules, such as YACs.

Applicants' Arguments

Applicants' argue the combined references do not satisfy the three elements of a prima facie case of obviousness (see Applicants response on page 7). Specifically, Applicants' argue the Brown-Smith combination does not teach a method for preparing an array of polynucleotides that is representative of a plurality of first oligonucleotides, and a polynucleotide array having this feature. Second, Applicants' argue there is no motivation to combine Brown and Smith, and states,

> In attempting to find the specific motivation required for a prima facie case, the Examiner notes that "Brown teaches a method of preparing an array of polynucleotides, including preparing an array of amplified polynucleotides." Office Action, page 4. To be more specific, Brown discloses the use of PCR to "randomly" amplify DNA for robotic spotting on substrates. Brown, col. 16, lines 9-22; col. 17, lines 46-55. However, nothing in Brown teaches or suggests any measures that would produce an amplification product (and, ultimately, target solution) wherein the starting polynucleotide sequences are present in approximately the same proportions as in the starting polynucleotide and thus representative of essentially the entire starting polynucleotide.

(page 8 of Applicants response).

Applicants continue by stating,

> The Examiner attempts to find motivation for ignoring Brown's teaching regarding "random amplification" and substituting Smith's ligation-mediated PCR amplification to produce DNA for arrays as follows: "Smith teaches that his PCR products can be used in arraying high-density grids (e.g., polynucleotide arrays) (pg. 26)." Office Action, page 5. Applicant respectfully submit that this misstates Smith's teaching. At page 26, Smith states "it is possible that pools of tagged PCR products from the ends of heterologous DNA segments cloned in YACS or cosmids could be employed for multiplex chromosome walking in clone libraries arrayed in high density grids." Chromosome walking is technique wherein sequences from the end of a clone of interest are

labeled and used as probes to identify additional clones that potentially contain flanking sequences. In this way, the sequence information for, e.g., a gene of interest can be extended. Accordingly, Smith teaches using ligation-mediated PCR products to probe conventionally created DNA arrays. Smith does not teach or suggest arraying ligation-mediated PCR products, as the Examiner states.

Finally, Applicants' argue there would not have been any reasonable expectation of success. In support of Applicants' argument, Applicants have submitted a 1.132 declaration from one of the inventors of the instant application, Dr. Donna G. Albertson. Applicants argue the declaration is "submitted to show that there are any number of amplification methods that could have been considered in connection with preparing target solutions for DNA arrays. In theory any of these methods might have worked. However, the inventors selected two amplification methods from among the myriad possibilities and found that one worked and one did not." (see page 11 of Applicants arguments). Furthermore, Applicants' argue, " that while she [Dr. Albertson] had an expectation regarding the likelihood of success of the shotgun cloning PCR method, she also appreciated that this particular field was relatively unpredictable." (see page 12 of Applicants' response). In summary, Applicants' argue that Dr. Albertson's declaration supports the proposition that the amplification approach that was expected to work the best (shotgun cloning) actually failed, and that the other amplification approach the inventors tried (ligation-mediated PCR) worked unexpectedly well. See Applicants arguments on page 12.

Response to Applicants' Arguments

Applicants' arguments and Dr. Albertson's declaration have been carefully considered, but are not persuasive for the following reasons.

Applicants' first argument, with respect to teaching all of the elements of the claims, is not persuasive for several reasons. First, Smith (page 22, Fig. 1) teaches the production of a plurality of target solutions, which are all derived from the same target DNA (i.e., representative of the corresponding first polynucleotide). The PCR products (shown in Figure 1) would contain DNA from the original target DNA (i.e., the first polynucleotide), and therefore, the plurality of PCR products would be representative of the starting polynucleotide. See also page 25, column 3. Furthermore, Smith teaches the PCR products can be arrayed on high-density grids (e.g., polynucleotide arrays) (pg. 26). Brown teaches a method of preparing an array of polynucleotides, including preparing an array of amplified polynucleotide products, but Brown does not teach preparing an array of specific PCR products, such as those from a ligation-mediated PCR reaction, which is taught by Smith. Accordingly, the combination of Brown and Smith would meet the limitations of both Claim 1 and Claim 20, as the combination teaches the method of Claim 1, which would produce the array of Claim 20.

Applicants' argument, with respect to motivation, is also not persuasive. First, Applicants are arguing limitations not present in the claims. Applicants' argue, "nothing in Brown teaches or suggests any measures that would produce an amplification product (and, ultimately, target solution) *wherein the starting polynucleotide sequences are present in approximately the same proportions* as in the starting polynucleotide and thus representative of essentially the entire starting polynucleotide." (See Applicants response on page 8). The italicized portion does not appear in the claims and therefore, this argument is not persuasive, as this is not a limitation required by the claims. Furthermore, the claims are silent as to whether the primers used are specific or random, and therefore, Applicants argument regarding Brown's

alleged teaching of random primers is also not persuasive. It is noted that the word "primer" is not present in Claim 1. Furthermore, it is also noted that Smith, not Brown, is being relied on for teaching the advantageous method of ligation-mediated PCR (encompassing steps a)-c) of Claim 1).

Applicants' argument that Smith does not provide adequate motivation is also not persuasive. First, Smith provides motivation for performing ligation-mediated PCR. For example, Smith teaches the advantages of performing ligation-mediated PCR are that "specific fragments can be isolated without any prior knowledge of the nucleotide sequence of the target" and furthermore, individual, unknown fragments can be amplified "from any DNA molecule ranging from about 50 to 250kb in size". (pg. 21) Additionally, as Applicant acknowledges, Smith teaches, "PCR products from the ends of heterologous DNA segments cloned in YACS or cosmids could be employed for multiplex chromosome walking in clone libraries arrayed in high density grids." (see Applicants' response on page 9). This expressly demonstrates that the PCR products of Smith can be used in conjunction with high-density grids (e.g., polynucleotide arrays). At this point, it is important to note the specific limitations of the claims, and namely that of step d) of Claim 1.

Step d) states, "*applying* target solutions comprising the amplification products to one or more substrates, wherein each target solution is *applied* to a distinct location on one substrate and/or target solutions are applied to different substrates that are combined to produce *an array of polynucleotides*."

(emphasis added)

First, the specification does not define what "applying" means, and therefore this can be interpreted broadly. Therefore, Smith's teaching that his target solutions comprising PCR products can be employed for multiplex chromosome walking in clone libraries arrayed in high density grids, would meet the limitation of "applying" the target solutions. Furthermore, the specification defines "array" as "a collection of elements, wherein each element is uniquely identifiable". See page 6, lines 10-11. Therefore, because Smith's PCR products can be employed for multiplex chromosome walking in clone libraries arrayed in high-density grids, this would necessarily mean that the elements of the chromosome-walking assay would be "uniquely identifiable". This assertion is supported by Applicants' conclusion that, "Accordingly, Smith teaches using ligation-mediated PCR products to probe conventionally created DNA arrays." (see Applicants' response on page 9). That is, as Applicants' assert, if Smith teaches that his PCR products "probe conventionally created DNA arrays", then his PCR products would necessarily be considered an "array of polynucleotides" (e.g., "uniquely identifiable" polynucleotides), because conventionally created DNA arrays are based on polynucleotides arrayed at distinct locations on a substrate, and therefore, the probing of these arrays would result in an array of polynucleotides (e.g., "uniquely identifiable" polynucleotides). In other words, Applicants appear to assert that the PCR products must be arrayed spotted on the substrate (e.g., not through a probe); however, the claims do not require this, as the claims only require that the target solutions be "applied" to a substrate to produce an "array" of polynucleotides. It is also noted that Brown teaches "applying target solutions comprising amplification products…to produce an array of polynucleotides", which is advantageous for analyzing a plurality of samples simultaneously (see above).

Applicants' argument that the Brown-Smith combination does not provide a reasonable expectation of success is also not persuasive. Applicants' arguments and Dr. Albertson's declaration have been considered, and it appears as if Applicants are arguing that the actual spotting of the PCR products occurs directly on an array, and that it is this "direct spotting" (e.g., not through a probe) that was unexpected at the time of the invention. As recited above, the claims do not require this, and therefore, the declaration is not commensurate in scope with the claims. For example, Dr. Albertson states:

> More specifically, *each target solution must, when spotted and hybridized with a labeled probe*, produce a signal that is essentially the same as the signal obtained from the starting polynucleotide." (page 2 of the Albertson declaration).
>
> "*Each P1/BAC DNA target solution was then hand-spotted onto a slide*...then hybridized with FITC-labeled BT474 (human tumor) DNA" (page 7 of the Albertson declaration).
>
> "Contrary to results obtained with the shotgun cloning approach, the ligation-mediated PCR approach worked unexpectedly well, *producing target solutions that, when spotted and hybridized with a labeled probe produced signal* that is essentially the same as the signal obtained from the starting polynucleotide."
>
> These passages seem to suggest that the target solution is spotted directly on the array,

and then a labeled probe can be hybridized to the spotted target solution, in order to detect tumors, for example. However, the claims are not directed to spotting the target solutions directly onto the array (and not through a probe, for example). Accordingly, the experiment detailed by the Albertson declaration is not commensurate in scope with the claims, and therefore is not persuasive. See MPEP 716.

Assuming that the claims and declaration do not purport to require that the target solution is spotted directly on the array (e.g., not through probes), Applicants arguments are still not persuasive. For example, the prior art of Sapolsky et al. (USPN 6,291,181) and Wyrick et al.

(USPN 6,410,243) teach the hybridization of ligation-mediated PCR products (from high molecular weight DNAs), to an array via probes, and therefore demonstrates that there was a reasonable expectation of success of hybridizing the PCR products of Smith onto an array, such as the array taught by Brown (See cols. 4-13 and Examples 1-3 of Sapolsky, and Figure 1 and cols. 2-9 of Wyrick).

Assuming that Applicants are purporting that there is not a reasonable expectation of success of spotting high molecular DNAs, such as BAC, directly onto the arrays (and not through probes, for example), Applicant's arguments are also not persuasive. For example, in 1998, the inventors of the instant application demonstrated that BAC DNA could be bound effectively and directly to an array (see Pinkel et al. (Nature Genetics (1998) 20:207-211, especially column 2 of page 210).

Accordingly, for these reasons and those of record, Applicants arguments are not deemed to be persuasive and therefore, the rejection is maintained.

4. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (US 5,807,522, cited in the IDS), in view of Smith (PCR Methods and Applications (1992) 2: 21-27, cited in the IDS), as applied to Claims 1, 3-16, 20, 23 and 25 above, and in further view of Gordon et al. (US 5,601,980, previously cited).

The teachings of Brown and Smith are presented above. The references do not teach the robotic spotting of the target solutions on the substrate.

Gordon et al. teaches a manufacturing method and apparatus for biological probe arrays using vision-assisted micropipetting. Specifically, Gordon teaches a robotically manipulated micropipette which is used for spotting biological samples onto an array (col. 3, ln. 59-60).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have further modified the method of Brown and Smith so as to have robotically spotted target solutions onto the substrate (i.e., array) in order to have achieved the benefits stated by Gordon of providing an accurate and cost effective spotting of miniscule volumes of biological material onto a substrate.

Applicants' Arguments

Applicants' argue Gordon does not teach the steps of Claim 1, "which result in approximately proportionate amplification of essentially all starting polynucleotide sequences". Also, Applicants' argue Gordon does not teach a motivation to modify Brown and Smith.

Response to Applicants' Arguments

Applicants' arguments have been considered, but are not persuasive for the following reasons. First, Applicants are arguing limitations not found in the claims. Specifically, the recitation of "which result in approximately proportionate amplification of essentially all starting polynucleotide sequences" is not found in any of the claims. Next, Gordon teaches the requisite motivation to robotically spot biological material (e.g., DNA) onto an array in order to provide an accurate and cost effective spotting of miniscule volumes of biological material onto a substrate (see col. 2, lines 46-52). Accordingly, given the advantages taught by Gordon, one skilled in the art would have been motivated to have robotically spotted the target solutions onto arrays for accurate and cost effective spotting of miniscule volumes of biological material onto a substrate.

Accordingly, this rejection is maintained.

5. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (US 5,807,522, cited in the IDS), in view of Smith (PCR Methods and Applications (1992) 2: 21-27, cited in the IDS), as applied to Claims 1, 3-16, 20, 23 and 25 above, and further in view of Stimpson et al. (Proc. Natl. Acad. Sci. USA (1995) 92: 6379-6383, previously cited).

The teachings of Smith and Brown are presented above. The references do not teach the method wherein at least one of the adapters includes an amino group.

Stimpson teaches the method of real-time detection of DNA hybridization and melting on oligonucleotide arrays by using optical wave-guides. Specifically, Stimpson teaches DNA chips (i.e. array), which are constructed by using 3'-amino-labeled oligonucleotides (pg. 6380). Furthermore, Stimpson teaches that these amino-labeled oligonucleotides are immobilized onto the chip (pg. 6380).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have further modified the method of Brown and Smith so as to have added an amino group to the adapter so as to have aided in the immobilization of the amplified polynucleotide onto the array.

Applicants' Arguments

Applicants' argue Stimpson does not remedy the deficiencies of Brown and Smith, does not teach the amplification steps of Claim 1, or any motivation to modify the teachings of Brown and Smith to produce the method of Claim 18.

Response to Applicants' Arguments

Applicants' arguments have been considered, but are not persuasive for the following reasons. First, the combined methods of Brown and Smith teach the method of Claim 1 (see

above). Furthermore, the fact that Stimpson does not itself teach a combination of the two methods only mitigates against using this reference as an anticipatory reference, not as evidence in reaching a conclusion of obviousness under 35 USC 103. Finally, Stimpson provides motivation that an amino group can be advantageously used to bind a nucleic acid to a solid support, and therefore, one of skill in the art would have added an amino group to the adapter of Brown and Smith so as to have aided in the immobilization of the amplified polynucleotide onto the array.

Accordingly, this rejection is maintained.

6. Claims 19, 21 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (US 5,807,522, cited in the IDS), in view of Smith (PCR Methods and Applications (1992) 2: 21-27, cited in the IDS), as applied to Claims 1, 3-16, 20, 23 and 25 above, and further in view of Cronin et al. (WO 97/43450, previously cited) or Pinkel et al. (USPN 5,837,196, previously cited).

The teachings of Brown and Smith are presented above. The references do not teach resuspending the target solutions with dimethyl sulfoxide (DMSO) at a concentration of about 20% by volume.

However, Cronin and Pinkel teach that it is advantageous to resuspend a target solution in DMSO in a concentration of about 20% volume. Specifically, Cronin teaches that the addition of a denaturing agent, such as DSMO in a concentration of at about 20%, to hybridization and/or wash buffers "greatly improves signal resolution in hybridization assays performed on substrate-bound oligonucleotide arrays (pg. 2 and 5-6). Pinkel teaches that the addition of DSMO in a

concentration of about 20% improves the attachment of nucleic acids to solid surfaces (col. 3, ln. 24-37 and cols. 11-12).

In view of the teachings of Cronin or Pinkel, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods of Brown and Smith so as to have included the steps of resuspending the target solution with DSMO in a concentration of at about 20%, in order to have achieved the benefits stated by Cronin of "greatly improv[ing] signal resolution in hybridization assays" or in order to have achieved the benefits stated by Pinkel of improving the attachment of nucleic acids to solid supports.

Applicants' Arguments

Applicants' argue Cronin and Pinkel do not remedy the deficiencies of Brown and Smith, do not teach the amplification steps of Claim 1, or provide motivation to produce the method of Claims 19, 21 and 24.

Response to Applicants' Arguments

Applicants' arguments have been considered, but are not persuasive for the following reasons. First, the combined methods of Brown and Smith teach the method of Claim 1 (see above). Furthermore, the fact that Cronin or Pinkel do not itself teach a combination of the two methods only mitigates against using these references as an anticipatory references, not as evidence in reaching a conclusion of obviousness under 35 USC 103. Finally, Cronin and Pinkel provide the requisite motivation to modify the teachings of Brown and Smith (see above).

Accordingly, the rejection is maintained.

Conclusion

7. No claims are allowable.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (571) 272-0788. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the primary examiner in charge of the prosecution of this case, Carla Myers, can be reached at (571) 272-0747. If attempts to reach Carla Myers are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Alexander H. Spiegler
February 11, 2004

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2/12/04